



NTP Nonneoplastic Lesion Atlas

Liver, Hepatocyte – Karyomegaly

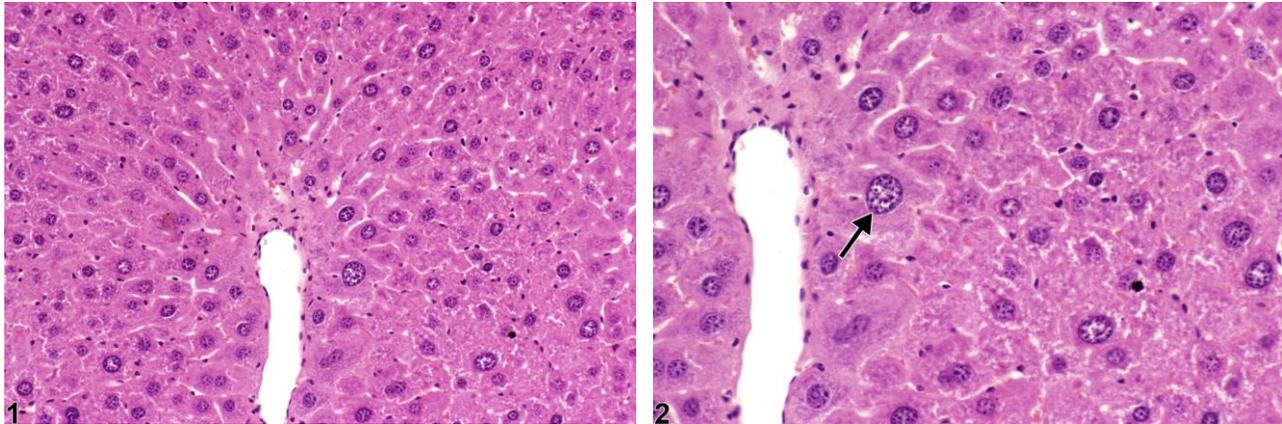


Figure Legend: **Figure 1** Karyomegaly in a female B6C3F1 mouse from a subchronic study. **Figure 2** Karyomegaly in a female B6C3F1 mouse from a subchronic study. Arrow indicates enlargement of hepatocyte cytoplasm and nucleus.

Comment: Though karyomegaly is predominantly a nuclear change, Figures 1 and 2 (arrow) show enlargement of both hepatocyte cytoplasm and nuclei. The change is throughout the hepatic lobule but is more prominent in the centrilobular areas. The increase in nuclear size is consistent with polyploidy, but in this subchronic study, the severity is significantly greater than one would expect at this age (~4.5 months). Although a liver weight increase was associated with enlarged hepatocytes in this study, the nonuniform hepatocyte enlargement plus the karyomegaly distinguish this change from hepatocyte enzyme induction. Spontaneous occurrence of karyocytomegaly is commonly seen in aging rodents and is not typically associated with increased liver weight. This aging change, often referred to as polyploidy, is more common in mice than in rats.

Recommendation: While some degree of nuclear enlargement is frequently seen in mice, particularly as an aging change, the degree of nuclear enlargement and the accompanying enlargement of hepatocytes shown in Figures 1 and 2 are not typically seen in control mice in prechronic studies. In this case it is a potential treatment effect and should be diagnosed and given a severity grade. It is typically not documented in chronic studies unless there is an



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obvious treatment-associated increase or decrease compared with concurrent controls. If the cytoplasm is enlarged but the nuclei are not, then the term “hypertrophy” should be used.

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Author:

Robert R. Maronpot, DVM, MS, MPH, DACVP, DABT, FIATP
Senior Pathologist
Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC